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| APPLICATION NO.  | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.                 | CONFIRMATION NO. |
|--|-------------|----------------------|-------------------------------------|------------------|
| 10/523,802   | 02/09/2005  | Mathias Locher       | 42804-212835                        | 6177             |
| 26694  | 7590        | 07/10/2009           |                                     |                  |
| VENABLE LLP<br>P.O. BOX 34385<br>WASHINGTON, DC 20043-9998 |             |                      | EXAMINER<br>BROOKS, KRISTIE LATRICE |                  |
|  |             |                      | ART UNIT                            | PAPER NUMBER     |
|  |             |                      | 1616                                |                  |
|  |             |                      | MAIL DATE                           | DELIVERY MODE    |
|  |             |                      | 07/10/2009                          | PAPER            |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                                      |                                      |  |
|------------------------------|--------------------------------------|--------------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/523,802 | <b>Applicant(s)</b><br>LOCHER ET AL. |  |
|                              | <b>Examiner</b><br>KRISTIE L. BROOKS | <b>Art Unit</b><br>1616              |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 09 February 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 17-23 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 17-23 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

### *Status of Application*

1. Claims 17-23 are pending.
  2. Receipt and consideration of Applicants remarks filed February 9, 2009 is acknowledged.
  3. Rejections not reiterated from the previous Office Action are hereby withdrawn.
- The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

### *New Grounds of Rejection*

#### *Claim Rejections - 35 USC § 112, 1<sup>st</sup>*

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
5. **Claims 17-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of respiratory diseases, allergic diseases, asthma, and/or chronic obstructive pulmonary diseases, does not reasonably provide enablement for the "prophylaxis" of the respiratory diseases, allergic diseases, asthma, and/or chronic obstructive pulmonary diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.**

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The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: 1) scope or breadth of the claims; 2) nature of the invention; 3) relative level of skill possessed by one of ordinary skill in the art; 4) state of, or the amount of knowledge in, the prior art; 5) level or degree of predictability, or a lack thereof, in the art; 6) amount of guidance or direction provided by the inventor; 7) presence or absence of working examples; and 8) quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure. When the above factors are weighed, it is the Examiner's position that one skilled in the art could not practice the invention without undue experimentation.

#### Scope or breadth of the claims

The scope of the claims is drawn to the treatment and prophylaxis of respiratory diseases, allergic diseases, asthma, and/or chronic obstructive pulmonary diseases comprising the step of administering loteprednol or pharmaceutically acceptable ester thereof and N-(3,5-dicholopyridin-4-yl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide or a pharmaceutically acceptable salt thereof to a subject in need of treatment.

#### Nature of the invention

The nature of the invention is directed to a method for the treatment and prophylaxis of respiratory diseases, allergic diseases, asthma, and/or chronic obstructive pulmonary diseases comprising the step of administering loteprednol or pharmaceutically acceptable ester thereof and N-(3,5-dicholopyridin-4-yl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide or a pharmaceutically acceptable salt thereof to a subject in need of treatment.

State of, or the amount of knowledge in, the prior art

The art teaches that although there are available treatments for conditions such as asthma, there is unlikely a cure to be developed in the near future (see Adcock et al., New targets for drug development in asthma, The Lancet, 372(9643):1073-87, 2008). There are treatments available for respiratory diseases such as lung cancer, however, patients should be aware that there is a limited change of cure (Mitchell et al., Lung cancer, Australian family Physician, 33(5):321-5, 2004).

Level or degree of predictability, or a lack thereof, in the art

Applicant broadly claims the "prophylaxis" of respiratory diseases, allergic diseases, asthma, and/or chronic obstructive pulmonary diseases comprising the step of administering loteprednol or pharmaceutically acceptable ester thereof and N-(3,5-dicholopyridin-4-yl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide or a pharmaceutically acceptable salt thereof to a subject in need of treatment. As defined

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by Merriam-Webster dictionary, prophylaxis is taken to mean prevention of a disease (see 892) and thus, the office interprets “prophylaxis” to be equivalent to prevention.

It is known in the art that there are various treatments available for the treatment of respiratory diseases. However, respiratory diseases such as asthma or lung cancer, are not curable. Furthermore, there are no examples in the instant specification drawn to the prevention of incurable respiratory diseases. Therefore, it cannot be established that the instant combination is cable of preventing incurable respiratory diseases. Thus, there is a high level of unpredictability as to whether the instant compounds will function to prevent all respiratory diseases.

Amount of guidance or direction provided by the inventor

The specification does not provide any guidance as to how to prevent respiratory diseases where there is no cure.

Presence or absence of working examples

The specification provides one example that disclosed the IC<sub>50</sub> values of DFHO and loteprednol for the GM-CSF release.

Quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure

One of ordinary skill in the art would have to conduct a myriad of experimentation to determine which compounds are effective at preventing respiratory diseases where

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there is no cure or there is a limited chance for a cure. As a result, one of ordinary skill in the art would be required to conduct an undue amount of experimentation.

For the foregoing reasons, Applicant is not enabled for "prophylaxis" of the respiratory diseases, allergic diseases, asthma, and/or chronic obstructive pulmonary diseases.

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claims 17-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodfellow et al. (US Pub No. 2004/0214805) in view of Szelenyi et al., Loteprednol

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etabonate: A soft steroid for the treatment of allergic diseases of the airways, *Drugs of Today*, 36(5):313, 2000 (Abstract).

Applicant claims a method for the treatment of respiratory diseases, allergic diseases, asthma, and/or chronic obstructive pulmonary diseases comprising the step of administering loteprednol or pharmaceutically acceptable ester thereof and N-(3,5-dicholopyridin-4-yl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide or a pharmaceutically acceptable salt thereof to a subject in need of treatment.

#### **Determination of the scope and content of the prior art**

##### **(MPEP 2141.01)**

Goodfellow et al. teach treating pulmonary diseases such as chronic obstructive pulmonary disease or asthma by administered a phosphodiesterase-4 (PDE-4) inhibitor in combination with an anti-inflammatory corticosteroid (see the abstract). Examples of PDE-4 inhibitors include AWD-12-281 (i.e. N-(3,5-dicholopyridin-4-yl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide) (see page 3 paragraph 0027). The compounds may be administered together or separately (see page 1 paragraph 0008). The formulation may be administered as an inhalable preparation (e.g. liquid or powder) or orally (see page 3 paragraphs 0032-0034). Goodfellow et al. also teach a method of treating a pulmonary disease in a mammal comprising administering an effective amount of a phosphodiesterase-4 (PDE-4) inhibitor in combination with an anti-inflammatory corticosteroid (see page 1 paragraph 0007).

**Ascertainment of the difference between the prior art and the claims**

**(MPEP 2141.02)**

Goodfellow et al. teach the combination of PDE-4 inhibitors and an anti-inflammatory but do not specifically teach loteprednol etabonate. This deficiency is cured by the teachings of Szelenyi et al.

Szelenyi et al. teach loteprednol etabonate as an antiallergic/antiasthmatic corticosteroid for the treatment of allergic diseases of the airways. It is highly suitable for nasal and pulmonary use (see the abstract).

**Finding of prima facie obviousness**

**Rational and Motivation (MPEP 2142-2143)**

One of ordinary skill in the art would have been motivated to do incorporate loteprednol etabonate into the combination taught by Goodfellow et al. because Goodfellow et al. suggest the combination of PDE-4 inhibitors and anti-inflammatory corticosteroids. Further, loteprednol etabonate is known for use in the treatment of allergic and respiratory diseases as suggested by Szelenyi et al.

Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute loteprednol etabonate into the method taught by Goodfellow et al. since it is an obvious variation of anti-inflammatory agents capable for use in the treatment of allergic and respiratory diseases taught by Goodfellow et al.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made because the prior art is fairly suggestive of the claimed composition.

### ***Response to Arguments***

Applicant's arguments with respect to claims 17-23 have been considered but are moot in view of the new ground(s) of rejection.

### ***Conclusion***

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kristie L. Brooks whose telephone number is (571) 272-9072. The examiner can normally be reached on M-F 8:30am-6:00pm Est..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

KB

/Johann R. Richter/

Supervisory Patent Examiner, Art Unit 1616